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Please search.
Making Humanized Antibodies
by. CDR: Grafting. [redacted]

[redacted]

See claims 1-13
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File 399:CA SEARCH_1967-1992 UD=11710
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?ds

Set	Items	Description
S1	16	HUMANIZED()ANTIBODIES/TI
S2	332298	ANTIBODIES! FROM 155
S3	2253	IMMUNOGLOBULIN VARIABLE REGION! FROM 155
S4	2253	S2 AND S3
S5	862	HUMANIZ?
S6	2005	HUMANIS?
S7	16	S4 AND (HUMANIZ? OR HUMANIS?)
S8	636823	ANTIBOD? FROM 5,73,399
S9	165469	IMMUNOGLOBULIN
S10	41830	IG
S11	113462	VARIABLE
S12	392448	REGION
S13	862	(IMMUNOGLOBULIN OR IG)(W)VARIABLE(W)REGION
S14	604	CDR
S15	67991	COMPLEMENTARY
S16	112646	DETERMINING
S17	63	COMPLEMENTARY(W)DETERMINING
S18	1904	HYPERVARIABLE
S19	392448	REGION
S20	747	(COMPLEMENTARY(W)DETERMINING OR HYPERVARIABLE)(W)REGION
S21	428778	ANTIBODY
S22	1469126	RELATED
S23	623755	BINDING
S24	544344	SITE? ?
S25	0	ANTIBODY(W)RELATED(W)BINDING(W)SITE? ?
S26	2161	(IMMUNOGLOBULIN OR IG)()VARIABLE()REGION OR CDR OR (COMPLEMENTARY()DETERMINING OR HYPERVARIABLE)()REGION OR ANTIBODY()RELATED()BINDING()SITE? ? FROM 5,73,399
S27	897	8 AND 26
S28	18	27 AND (5 OR 6)
S29	34	28 OR 7
S30	21	RD (unique items)
S31	21	Sort S30/ALL/PY,D

synonyn for CDR

synonyms for CDR

?t31/7/1-21

31/7/1 (Item 1 from file: 5)
9568885 BIOSIS Number: 94073885
HUMANIZED OKT3 *ANTIBODIES* SUCCESSFUL TRANSFER OF IMMUNE MODULATING PROPERTIES AND IDIOTYPE EXPRESSION
WOODLE E S; THISTLEWAITE J R; JOLLIFFE L K; ZIVIN R A; COLLINS A; ADAIR J A; BODMER M; ATHWAL D; ALEGRE M-L; BLUESTONE J A
SECT. ORGAN TRANSPLANTATION, DEP. SURGERY, WASH. UNIV. SCH. MED., ONE BARNES HOSP. PLAZA, QUEENY TOWER, SUITE 6107, ST. LOUIS, MO. 63110.
J IMMUNOL 148 (9). 1992. 2756-2763. CODEN: JOIMA
Full Journal Title: Journal of Immunology
Language: ENGLISH

. .*Antibodies* that possess the Ag-binding regions of OKT3 within the context of a human framework (Hu-OKT3 Ab) offer distinct advantages for optimizing anti-CD3 mAb therapy. First, manipulation of Ab genes to produce *humanized*. Ab that retain Ag-binding activity may circumvent antigenicity problems. Second, Ab gene engineering provides a means for modifying functional properties, including T cell activation and immune suppression. The purpose of this study was to determine the functional properties of Hu-OKT3 Ab and to compare the functional properties and idiotypes of Hu-OKT3 Ab to those of maurine OKT3. Three Hu-OKT3 IgG4 aAb, a chimeric OKT3 *antibody* (cOKT3-1) (grafted sequences comprising all OKT3 VH and VL regions) and two complementarity determining region (*CDR*)-grafted *antibodies* , gOKT3-5 and gOKT3-6 (grafted sequences comprising only OKT3 VH and VL *CDR* and some framework amino acids, were analyzed. Initial studies demonstrated that the cOKT3 and gOKT3-5 Ab bound selectively to T cells and competitively inhibited OKT3-FITC binding with avidities similar to that of murine OKT3. binding avidity of the gOKT3-6 Ab was markedly less than that of the other Hu-OKT3 Ab. Serologic analysis suggested that cOKT3 and gOKT3-5 Ab possess idiotypes (combining sites) similar to murine OKT3. C cell activation potency of all three Hu-OKT3 Ab was assessed by proliferation, induction of activation marker expression (IL-2R and Leu 23), and lymphokine production (TNF-.alpha. and IFN-.gamma.). The cOKT3 and gOKT3-5 Ab demonstrated T cell activation potencies similar to murine OKT3 as assessed by each parameter. CD3 coating and modulation by these two Ab was effective but somewhat less potent than that observed with OKT3. Finally, cOKT3 and gOKT3-5 Ab both inhibited CTL activity comparably to murine OKT3. In conclusion, these studies indicate that gOKT3-5 and cOKT3 Ab possess immune modulating properties similar to murine OKT3 and thus offer attractive alternatives to murine OKT3 for in vivo therapy.

31/7/2 (Item 2 from file: 155)
08124424 92262424

Humanization of an anti-p185HER2 antibody for human cancer therapy.

Carter P; Presta L; Gorman CM; Ridgway JB; Henner D; Wong WL; Rowland AM; Kotts C; Carver ME; Shepard HM

Department of Protein Engineering, Genentech Inc., South San Francisco, CA 94080.

Proc Natl Acad Sci U S A (UNITED STATES) May 15 1992, 89 (10) p4285-9, ISSN 0027-8424 Journal Code: PV3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The murine monoclonal antibody mumAb4D5, directed against human epidermal growth factor receptor 2 (p185HER2), specifically inhibits proliferation of human tumor cells overexpressing p185HER2. However, the efficacy of mumAb4D5 in human cancer therapy is likely to be limited by a human anti-mouse antibody response and lack of effector functions. A "*humanized* " antibody, humAb4D5-1, containing only the antigen binding loops from mumAb4D5 and human variable region framework residues plus IgG1 constant domains was constructed. Light- and heavy-chain variable regions were simultaneously *humanized* in one step by "gene conversion mutagenesis" using 311-mer and 361-mer preassembled oligonucleotides, respectively. The humAb4D5-1 variant does not block the proliferation of human breast carcinoma SK-BR-3 cells, which overexpress p185HER2, despite tight antigen binding (Kd = 25 nM). One of seven additional *humanized* variants designed by molecular modeling (humAb4D5-8) binds the p185HER2 antigen 250-fold and 3-fold more tightly than humAb4D5-1 and mumAb4D5, respectively. In addition, humAb4D5-8 has potency comparable to the murine antibody in blocking SK-BR-3 cell proliferation. Furthermore, humAb4D5-8 is much more efficient in supporting antibody-dependent cellular cytotoxicity against SK-BR-3 cells than mumAb4D5, but it does not efficiently kill WI-38 cells, which express p185HER2 at lower levels.

31/7/3 (Item 3 from file: 155)
08081267 92219267
Antibody framework residues affecting the conformation of the hypervariable loops.
Foote J; Winter G
MRC Laboratory of Molecular Biology, Cambridge, England.
J Mol Biol (ENGLAND) Mar 20 1992, 224 (2) p487-99, ISSN 0022-2836 Journal Code: J6V
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Rodent monoclonal antibodies have been "*humanized*" or "reshaped" for therapy by transplanting the antigen-binding loops from their variable domains onto the beta-sheet framework regions of human antibodies. However, additional substitutions in the human framework regions are sometimes required for high affinity antigen binding. Here we describe antigen binding by a reshaped antibody derived from the mouse anti-lysozyme antibody D1.3, and several variants in which point mutations had been introduced into framework positions to improve its affinity. The affinities were determined from the relaxation kinetics of reactant mixtures using quenching of fluorescence that occurs upon formation of the antibody-antigen complex. The dissociation constant of lysozyme ranged from 3.7 nM (for D1.3) to 260 nM. Measurement of antibody-antigen association kinetics using stopped-flow showed that D1.3 and most of the reshaped antibodies had bimolecular rate constants of 1.4 x 10(6) s-1 M-1, indicating that differences in equilibrium constant were predominantly due to different rates of dissociation of lysozyme from immune complexes. Mutations in a triad of heavy chain residues, 27, 29 and 71, contributed 0.9 kcal/mol in antigen binding free energy, and a Phe to Tyr substitution of light chain residue 71 contributed an additional 0.8 kcal/mol. The combined effect of all these mutations brought the affinity of the reshaped antibody to within a factor of 4 of D1.3. All of these substitutions were in the beta-sheet framework closely underlying the complementarity-determining regions, and do not participate in a direct interaction with antigen. The informed selection of residues in such positions may prove essential for the success of loop transplants in antibodies. Variation of these sites may also have a role in shaping the diversity of structures found in the primary repertoire, and in affinity maturation.

31/7/4 (Item 4 from file: 155)
08010135 92148135
Chimeric and *humanized* antibodies with specificity for the CD33 antigen.
Co MS; Avdalovic NM; Caron PC; Avdalovic MV; Scheinberg DA; Queen C
Protein Design Labs, Inc., Mountain View, CA 94043.
J Immunol (UNITED STATES) Feb 15 1992, 148 (4) p1149-54, ISSN 0022-1767 Journal Code: IFB
Contract/Grant No.: NIH CA55349
Languages: ENGLISH
Document type: JOURNAL ARTICLE
L and H chain cDNAs of M195, a murine mAb that binds to the CD33 Ag on normal and leukemic myeloid cells, were cloned. The cDNAs were used in the construction of mouse/human IgG1 and IgG3 chimeric antibodies. In addition, *humanized* antibodies were constructed which combined the complementarity-determining regions of the M195 antibody with human framework and constant regions. The human framework was chosen to maximize homology with the M195 V domain sequence. Moreover, a computer model of M195 was used to identify several framework amino acids that are likely to interact with the complementarity-determining regions, and these residues

were also retained in the *humanized* antibodies. Unexpectedly, the *humanized* IgG1 and IgG3 M195 antibodies, which have reshaped V regions, have higher apparent binding affinity for the CD33 Ag than the chimeric or mouse antibodies.

31/7/5 (Item 5 from file: 155)
07996790 92134790
Gene conversion of immunoglobulin variable regions in mutagenesis cassettes by replacement PCR mutagenesis.
Near RI
Cellular and Molecular Research Laboratory, Massachusetts General Hospital, Boston 02144.
Biotechniques (UNITED STATES) Jan 1992, 12 (1) p88-97, ISSN 0736-6205 Journal Code: AN3
Contract/Grant No.: HL-19259
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A technique, Replacement PCR Mutagenesis, was developed to replace one immunoglobulin variable region (V) in a M13 phage cassette with a different, homologous V. This allows the use of the same mutagenesis and subsequent expression vectors for many V regions or V segments. The method combines PCR of V fragments and in vitro mutagenesis. Primers homologous to 3′ and 5′ ends of both V regions initiate PCR synthesis of the V DNA fragment (donor) that will replace the V region (recipient) in M13. Donor V PCR DNA may originate from mRNA, cloned V genes or genomic templates. The donor V PCR DNA is denatured and annealed to the M13 cassette containing the recipient V to be supplanted. The second strand is synthesized, transfected into bacteria and mutant plaques selected by hybridization. Since restriction sites in primers are not required, altered primer-encoded amino acids are avoided. Further, the PCR donor piece can be of any length if it shares homology with the recipient gene. This allows construction and expression of complete gene replacements and chimeras. This method is also applicable to V "*humanization* " and studying sets of homologous genes containing polymorphic or evolutionary disparities. The potential uses of the technique are discussed.

31/7/6 (Item 6 from file: 5)
8779979 BIOSIS Number: 42004979
IMMUNOHISTOCHEMICAL CHARACTERIZATION OF THE *CDR*-GRAFTED *HUMANIZED* MONOCLONAL *ANTIBODY* BW 431-26 HUMAB PRECLINICAL STUDY
MASCHEK W; BOSSLET K
INST. NUCLEARMED., LINZ BEHRING RES. LABS, MARBURG, FRG.
EUROPEAN ASSOCIATION OF NUCLEAR MEDICINE CONGRESS, VIENNA, AUSTRIA, SEPTEMBER 1-5, 1991. EUR J NUCL MED 18 (8). 1991. 546. CODEN: EJNMD
Language: ENGLISH

31/7/7 (Item 7 from file: 5)
8563624 BIOSIS Number: 92028624
POLYMERASE CHAIN REACTION FACILITATES THE CLONING *CDR*-GRAFTING AND RAPID EXPRESSION OF A MURINE MONOCLONAL *ANTIBODY* DIRECTED AGAINST THE CD18 COMPONENT OF LEUKOCYTE INTEGRINS
DAUGHERTY B L; DEMARTINO J A; LAW M-F; KAWKA D W; SINGER I I; MARK G E
DEP. CELL. MOL. BIOL., MERCK SHARP DOHME RES. LAB., RAHWAY, N.J. 07065, USA.
NUCLEIC ACIDS RES 19 (9). 1991. 2471-2476. CODEN: NARHA
Full Journal Title: Nucleic Acids Research
Language: ENGLISH
Two novel approaches of recombinant PCR technology were employed to graft the complementarity determining regions from a murine monoclonal *antibody* (mAb) onto human *antibody* frameworks. One approach relied on the

availability of cloned human variable region templates, whereas the other strategy was dependent only on human variable region protein sequence data. The transient expression of recombinant *humanized* *antibody* was driven by the adenovirus major late promoter and was detected 48 hrs post-transfection into non-lymphoid mammalian cells. The application of these new approaches enables the expression of a recombinant *humanized* *antibody* just 6 weeks after initiating the cDNA cloning of the murine mAB.

31/7/8 (Item 8 from file: 155)
08049594 92187594
Humanization of a mouse monoclonal antibody by CDR-grafting: the importance of framework residues on loop conformation.
Kettleborough CA; Saldanha J; Heath VJ; Morrison CJ; Bendig MM
Medical Research Council Collaborative Centre, London, UK.
Protein Eng (ENGLAND) Oct 1991, 4 (7) p773-83, ISSN 0269-2139
Journal Code: PR1
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A mouse monoclonal antibody (mAb 425) with therapeutic potential was ' *humanized* ' in two ways. Firstly the mouse variable regions from mAb 425 were spliced onto human constant regions to create a chimeric 425 antibody. Secondly, the mouse complementarity-determining regions (CDRs) from mAb 425 were grafted into human variable regions, which were then joined to human constant regions, to create a reshaped human 425 antibody. Using a molecular model of the mouse mAb 425 variable regions, framework residues (FRs) that might be critical for antigen-binding were identified. To test the importance of these residues, nine versions of the reshaped human 425 heavy chain variable (VH) regions and two versions of the reshaped human 425 light chain variable (VL) regions were designed and constructed. The recombinant DNAs coding for the chimeric and reshaped human light and heavy chains were co-expressed transiently in COS cells. In antigen-binding assays and competition-binding assays, the reshaped human antibodies were compared with mouse 425 antibody and to chimeric 425 antibody. The different versions of 425-reshaped human antibody showed a wide range of avidities for antigen, indicating that substitutions at certain positions in the human FRs significantly influenced binding to antigen. Why certain individual FR residues influence antigen-binding is discussed. One version of reshaped human 425 antibody bound to antigen with an avidity approaching that of the mouse 425 antibody.

31/7/9 (Item 9 from file: 155)
07969093 92107093
Humanization of monoclonal antibodies.
Gussow D; Seemann G
Methods Enzymol (UNITED STATES) 1991, 203 p99-121, ISSN 0076-6879
Journal Code: MVA
Languages: ENGLISH
Document type: JOURNAL ARTICLE

31/7/10 (Item 10 from file: 155)
07953750 92091750
Construction, expression and characterization of *humanized* antibodies directed against the human alpha/beta T cell receptor.
Shearman CW; Pollock D; White G; Hehir K; Moore GP; Kanzy EJ; Kurrle R
Genzyme Corporation, Framingham, MA 01701.
J Immunol (UNITED STATES) Dec 15 1991, 147 (12) p4366-73, ISSN 0022-1767 Journal Code: IFB
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Completely *humanized* antibodies with specificity for the human alpha/beta TCR have been produced by genetic engineering. The L and H chain V region exons encoding the murine mAb BMA 031 CD regions and human EU framework regions were synthesized and replaced into previously isolated genomic fragments. These fragments were inserted into mammalian expression vectors containing the human kappa and gamma 1 C region exons. Two variants were constructed each containing selected BMA 031 amino acids within the human frameworks. The *humanized* genes were transfected into Sp2/0 hybridoma cells by electroporation and transfectomas secreting *humanized* antibody were isolated. Levels of antibody expression up to 7 pg/cell/24 h were obtained. The *humanized* antibody, BMA 031-EUCIV2, competed poorly with murine BMA 031 for binding to T cells. BMA 031-EUCIV3, however, bound specifically to T cells and competed effectively with both the murine BMA 031 antibody and a previously constructed chimeric BMA 031 antibody for binding to these cells. The relative affinity of BMA 031-EUCIV3 was about 2.5 times lower than BMA 031. The ability to promote antibody dependent cell-mediated cytolysis was significantly enhanced with the engineered antibodies as compared to murine BMA 031. *Humanized* BMA 031 is a clinically relevant, genetically engineered antibody with potential uses in transplantation, graft vs host disease, and autoimmunity.

31/7/11 (Item 11 from file: 155)
07909485 92047485

Antigenicity of mouse monoclonal antibodies. A study on the variable region of the heavy chain.

Olsson PG; Hammarstrom L; Smith CI
Department of Clinical Immunology, Karolinska Institute, Huddinge University Hospital, Sweden.

J Theor Biol (ENGLAND) Jul 7 1991, 151 (1) p111-22, ISSN 0022-5193 Journal Code: K8N
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Mouse monoclonal antibodies (Mabs) against human tumour antigens are currently used in therapy, but up to 50% of the patients receiving treatment form anti-Mab antibodies thus reducing the efficiency of the treatment. One attempt to minimize the immunogenicity of the mouse Mabs is to "*humanize* " them by replacing the constant part of the molecule with the human equivalent by genetic engineering. However, this does not reduce the immunogenicity of the variable part of the antibody. Some variable regions may be expected to be less antigenic than others. We therefore compared consensus sequences for the 11 mouse VH families with the human VH sequences published so far. Theoretical antigenicity predictions (hydrophilicity, flexibility, surface accessibility and relative antigenicity) were made and two families; VH I(J558) and VH XI (CP5 B5-3) were predicted to be immunogenic by all four methods. One family, VH X (MRL-DNA4), was not predicted to be immunogenic by any of the four methods. The residues predicted to form antigenic epitopes in the two families VH II (Q52) and VH III (36-60) are predicted not to be exposed on the surface of the antibody molecule and may therefore not be immunogenic.

31/7/12 (Item 12 from file: 5)
7905670 BIOSIS Number: 40106670

QH506.J67

CHIMERIC MOUSE-HUMAN AND *CDR*-GRAFTED *ANTIBODIES* TO HUMAN IL2 RECEPTOR

WEIDLE U H; RUSSMANN E; LENZ H; KALUZA B
BOEHRINGER MANNHEIM GMBH, NONNENWALD 2, D-8122 PENZBERG, FRG.

MEETING ON MOLECULAR BIOLOGY AND THE IMMUNOPATHOGENESIS OF RHEUMATOID ARTHRITIS HELD AT THE 20TH ANNUAL MEETING OF THE KEYSTONE SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, LAKE TAHOE, CALIFORNIA, USA, MARCH 15-21, 1991. J CELL BIOCHEM SUPPL 15 (PART E). 1991. 186. CODEN: JCBSD
Language: ENGLISH

31/7/13 (Item 13 from file: 155)
07899816 92037816
A *humanized* monovalent CD3 antibody which can activate homologous complement.
Routledge EG; Lloyd I; Gorman SD; Clark M; Waldmann H
Department of Pathology, Cambridge University.
Eur J Immunol (GERMANY) Nov 1991, 21 (11) p2717-25, ISSN 0014-2980 Journal Code: EN5
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The rat monoclonal antibody (mAb) YTH12.5, specific for the CD3 antigen complex on human T cells has been modified in order to improve its efficacy in human therapy. With the aim of rendering it less immunogenic, it has been *humanized* using the method of framework grafting. During this process sequence analysis of the YTH12.5 VL gene indicated that it was of the lambda subclass, however, it was markedly dissimilar from previously published rat and mouse V lambda gene sequences and may represent a new V lambda gene family. The *humanization* of this light chain represents the first successful reshaping of a lambda light chain V region. To improve the effector function of the antibody we have created a monovalent form (1 Fab, 1 Fc) using a novel method involving the introduction of an N-terminally truncated human IgG1 heavy chain gene into cells producing the *humanized* CD3 mAb. Comparison of the mono- and bivalent *humanized* mAb in a complement-mediated cell lysis assay revealed that the monovalent antibody mediated lysis of human T cell blasts whereas the bivalent form did not. The availability of a *humanized*, complement-fixing CD3 mAb may improve opportunities for human therapy, in the management of organ rejection, autoimmunity and the treatment of T cell lymphoma.

31/7/14 (Item 14 from file: 155)
07768736 91287736
A possible procedure for reducing the immunogenicity of antibody variable domains while preserving their ligand-binding properties.
Get This
Padlan EA
Laboratory of Molecular Biology, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892.
Mol Immunol Apr-May 1991, 28 (4-5) p489-98, ISSN 0161-5890 Journal Code: NG1
QR180.I52.
Languages: ENGLISH
Document type: JOURNAL ARTICLE
It is proposed to reduce the immunogenicity of allogeneic antibody variable domains, while preserving ligand-binding properties, by reducing their antigenicity through replacement of the exposed residues in the framework regions which differ from those usually found in host antibodies. The results of a comparison of representative murine antibody sequences with those of human origin suggest that the number of residues that need to be replaced to "*humanize*" those antibodies could be small.
Get This

31/7/15 (Item 15 from file: 155)
07757287 91276287
Immunoglobulin complementarity-determining region grafting by recombinant polymerase chain reaction to generate *humanised* monoclonal antibodies.
Lewis AP; Crowe JS
Department of Cell Biology, Wellcome Research Laboratories, Beckenham, Kent, U.K.
Gene May 30 1991, 101 (2) p297-302, ISSN 0378-1119 Journal Code: FOP
QH 442.B43
Languages: ENGLISH

Document type: JOURNAL ARTICLE
We describe an approach to rapidly generate *humanised* monoclonal antibodies by grafting rodent complementarity-determining regions onto human immunoglobulin frameworks using recombinant polymerase chain reaction (PCR) methodology. The approach was applied to grafting a rat complementarily-determining region onto a human framework and amplifying the entire *humanised* heavy chain. The terminal oligodeoxyribonucleotide primers incorporated restriction sites to allow forced cloning into plasmid vectors for sequencing and expression. No nucleotide errors were introduced into the 1463-bp sequence even after sequential applications of PCR.

31/7/16 (Item 16 from file: 155)
07668893 91187893
Humanized antibodies for antiviral therapy.
Co MS; Deschamps M; Whitley RJ; Queen C
Protein Design Labs, Inc., Mountain View, CA 94043.
Proc Natl Acad Sci U S A Apr 1 1991, 88 (7) p2869-73, ISSN 0027-8424
Journal Code: PV3
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Antibody therapy holds great promise for the treatment of cancer, autoimmune disorders, and viral infections. Murine monoclonal antibodies are relatively easy to produce but are severely restricted for therapeutic use by their immunogenicity in humans. Production of human monoclonal antibodies has been problematic. *Humanized* antibodies can be generated by introducing the six hypervariable regions from the heavy and light chains of a murine antibody into a human framework sequence and combining it with human constant regions. We *humanized*, with the aid of computer modeling, two murine monoclonal antibodies against herpes simplex virus gB and gD glycoproteins. The binding, virus neutralization, and cell protection results all indicate that both *humanized* antibodies have retained the binding activities and the biological properties of the murine monoclonal antibodies.

31/7/17 (Item 17 from file: 399)
117024688 CA: 117(3)24688r PATENT
Humanized complementarily-determing region (CDR)-grafted antibodies to intercellular adhesion molecule-1 (ICAM-1), methods of preparation and usage thereof
INVENTOR(AUTHOR): Adair, John Robert; Athwal, Diljeet Singh; Rothlein, Robert A.
LOCATION: UK,
ASSIGNEE: Celltech Ltd.; Boehringer Ingelheim Pharmaceuticals, Inc.
PATENT: PCT International ; WO 9116927 A1 DATE: 911114
APPLICATION: WO 91US2942 (910429) *GB 909549 (900427)
PAGES: 81 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A; C07K-015/28B DESIGNATED COUNTRIES: AT; AU; BB; BG; BR; CA; CH; DE; DK; ES; FI; GB; HU; JP; KP; KR; LK; LU; MC; MG; MW; NL; NO; PL; RO; SD; SE; SU; US
DESIGNATED REGIONAL: AT; BE; BF; BJ; CF; CG; CH; CM; DE; DK; ES; FR; GA; GB; GR; IT; LU; ML; MR; NL; SE; SN; TD; TG
SECTION:
CA215003 Immunochemistry
CA201XXX Pharmacology
CA203XXX Biochemical Genetics
IDENTIFIERS: humanized antibody intercellular adhesion mol 1, inflammation inhibitor humanized antibody ICAM1, asthma inhibitor humanized antibody ICAM1, AIDS virus humanized antibody ICAM1, virucide humanized antibody ICAM1, diagnosis humanized antibody ICAM1
DESCRIPTORS:
Dermatitis...

antibody to intercellular adhesion mol.-1
Mouse...
monoclonal antibody R6-5-D6 of, in humanized antibody to intercellular adhesion mol.-1 prodn.
Sepsis and Septicemia...
multiple organ injury syndrome secondary to, inflammation of, treatment of, humanized antibody to intercellular adhesion mol.-1 for
Protein sequences...
of monoclonal antibody R6-5-D6 heavy and light chain components for humanized antiintercellular adhesion mol.-1 antibody
Plasmid and Episome...
pAL5, in grafted humanized antibody to intercellular adhesion mol.-1 prodn.
Plasmid and Episome...
pAL6, in grafted humanized antibody to intercellular adhesion mol.-1 prodn.
Plasmid and Episome...
pBJ1, in grafted humanized antibody to intercellular adhesion mol.-1 prodn.
Kidney,transplant... Organ,transplant... Transplant and Transplantation...
rejection of, inflammation of, treatment of, humanized antibody to intercellular adhesion mol.-1 for
Antibodies,monoclonal...
R6-5-D6, of mouse, in humanized antibody to intercellular adhesion mol.-1 prodn.
Organ,disease, multiple organ failure...
secondary to septicemia or trauma, treatment of, humanized antibody to intercellular adhesion mol.-1 for
Temperature effects,biological...
thermal injury, inflammation of, treatment of, humanized antibody to intercellular adhesion mol.-1 for
Perfusion,re-...
tissue injury from, treatment of, humanized antibody to intercellular adhesion mol.-1 for
Lymphokines and Cytokines...
toxicity induced by, inflammation of, treatment of, humanized antibody to intercellular adhesion mol.-1 for
Neoplasm inhibitors...
toxin-derivatized humanized antibody to intercellular adhesion mol.-1, for intercellular adhesion mol.-1-expressing tumor cell
Leukocyte,granulocyte...
transfusion-assocd. syndrome, treatment of, humanized antibody to intercellular adhesion mol.-1 for
Allergy,delayed hypersensitivity...
treatment of, humanized antibody to intercellular adhesion mol.-1 for
Picornaviridae... Virus,animal, Coxsackie A... Virus,animal, human immunodeficiency... Virus,animal, human immunodeficiency 1... Virus,animal, Mengo... Virus,animal, rhino-...
treatment of infection with, with humanized antibody to intercellular adhesion mol.-1
Hematopoietic precursor cell...
tumorous, metastasis of, inhibition of, chimeric antibody to intercellular adhesion mol.-1
Genetic vectors...
with DNA for antibody heavy and light chains, in humanized antibody to intercellular adhesion mol.-1 prodn.

CAS REGISTRY NUMBERS:

142007-78-1 142007-79-2 142007-80-5 142007-81-6 142007-82-7 142007-83-8 142007-85-0 amino acid sequence of 142007-84-9 amino acid sequence of, humanized antibody to intercellular

adhesion mol.-1 in relation to
140876-28-4 140876-29-5 142007-86-1 142007-87-2 amino acid sequence of, humanized antibody to intercellular adhesion mol.-1 prodn. in relation to
140857-88-1 142008-94-4 nucleotide sequence of, humanized antibody to intercellular adhesion mol.-1 prodn. in relation to
140857-89-2 142008-93-3 nucleotide sequence of, humanized antibody to intercellular adhesion mol.01 prodn. in relation to

31/7/18 (Item 18 from file: 155)
07449972 90356972
Immunoglobulin V regions of a bactericidal anti-Neisseria meningitidis outer membrane protein monoclonal antibody.
Larrick JW; Coloma MJ; del Valle J; Fernandez ME; Fry KE; Gavilondo-Cowley JV
Genelabs Inc., Redwood City, California.
Scand J Immunol Aug 1990, 32 (2) p121-8, ISSN 0300-9475
Journal Code: UCW
Languages: ENGLISH
Document type: JOURNAL ARTICLE
C6 is a potentially therapeutic murine monoclonal antibody that recognizes the class 1 outer membrane protein of Neisseria meningitidis. C6 specifically immunoblots this antigen and augments in vitro killing of N. meningitidis bacteria. We describe a general method of obtaining the heavy and light chain variable-region sequence from immunoglobulin-secreting cells. The method uses mixed polymerase chain reaction (PCR) primers designed from the 5′ end of the framework 1 (FR1) sequences of the heavy and light chains, and 3′-end primers for constant-region conserved sequences. The method has been applied to the cloning and sequencing of the variable region of C6 to construct a *humanized* monoclonal antibody. Rapid amplification and sequencing of variable regions by this general method have multiple applications in the study of the immune response to infectious diseases.

31/7/19 (Item 19 from file: 155)
07292738 90199738
Cloning of the genes for T84.66, an antibody that has a high specificity and affinity for carcinoembryonic antigen, and expression of chimeric human/mouse T84.66 genes in myeloma and Chinese hamster ovary cells.
Neumaier M; Shively L; Chen FS; Gaida FJ; Ilgen C; Paxton RJ; Shively JE; Riggs AD
Division of Biology, Beckman Research Institute of the City of Hope, Duarte, California 91010.
Cancer Res Apr 1 1990, 50 (7) p2128-34, ISSN 0008-5472
Journal Code: CNF
Contract/Grant No.: CA 43904
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Carcinoembryonic antigen (CEA) is one of the best characterized tumor-associated antigens and is extensively used in the in vitro immunodiagnosis of human colon adenocarcinomas. Among a number of anti-CEA monoclonal antibodies, the murine monoclonal antibody T84.66 shows the highest specificity and affinity for CEA and has been used successfully for in vivo tumor imaging in mice and humans. We report here the cloning and sequencing of the genes coding for monoclonal antibody T84.66 and the amino acid sequence of the variable regions for the heavy and light chains. We also report the construction of mouse/human chimeric IgG1 antibody genes using T84.66 variable region genes and human constant region genes. The resulting chimeric gene constructs were transfected into murine myeloma

cells (Sp2/0) by electroporation and into Chinese hamster ovary cells by lipofection. The chimeric antibodies obtained exhibited the same specificity and affinity for CEA as that of the T84.66 immunoglobulin produced by the murine hybridoma cell line. Antibody concentrations in culture medium supernatants were clonally variable but similar (15-480 ng/ml) for both Sp2/0 and Chinese hamster ovary transfectants; the average production by Chinese hamster ovary transfectants was only 3-5-fold less than Sp2/0 transfectants. Ascites production of Sp2/0 transfectants is sufficiently high (900 micrograms/ml) for initial in vivo studies with *humanized* T84.66.

31/7/20 (Item 20 from file: 155)
07192290 90099290

A *humanized* antibody that binds to the interleukin 2 receptor.

Queen C; Schneider WP; Selick HE; Payne PW; Landolfi NF; Duncan JF; Avdalovic NM; Levitt M; Junghans RP; Waldmann TA

Protein Design Labs, Palo Alto, CA 94304.

Proc Natl Acad Sci U S A Dec 1989, 86 (24) p10029-33, ISSN 0027-8424 Journal Code: PV3

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The anti-Tac monoclonal antibody is known to bind to the p55 chain of the human interleukin 2 receptor and to inhibit proliferation of T cells by blocking interleukin 2 binding. However, use of anti-Tac as an immunosuppressant drug would be impaired by the human immune response against this murine antibody. We have therefore constructed a "*humanized*" antibody by combining the complementarity-determining regions (CDRs) of the anti-Tac antibody with human framework and constant regions. The human framework regions were chosen to maximize homology with the anti-Tac antibody sequence. In addition, a computer model of murine anti-Tac was used to identify several amino acids which, while outside the CDRs, are likely to interact with the CDRs or antigen. These mouse amino acids were also retained in the *humanized* antibody. The *humanized* anti-Tac antibody has an affinity for p55 of 3 x 10(9) M-1, about 1/3 that of murine anti-Tac.

31/7/21 (Item 21 from file: 155)
06533056 88178056

Reshaping human antibodies: grafting an antilysozyme activity.

Verhoeyen M; Milstein C; Winter G

Medical Research Council Laboratory of Molecular Biology, Cambridge, England.

Science Mar 25 1988, 239 (4847) p1534-6, ISSN 0036-8075 Journal Code: UJ7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The production of therapeutic human monoclonal antibodies by hybridoma technology has proved difficult, and this has prompted the "*humanizing*" of mouse monoclonal antibodies by recombinant DNA techniques. It was shown previously that the binding site for a small hapten could be grafted from the heavy-chain variable domain of a mouse antibody to that of a human myeloma protein by transplanting the hypervariable loops. It is now shown that a large binding site for a protein antigen (lysozyme) can also be transplanted from mouse to human heavy chain. The success of such constructions may be facilitated by an induced-fit mechanism.

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SYSTEM:OS  - DIALOG OneSearch
  File 351:Derwent World Patents Index Latest
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 **FILE351: Formats 32,33,35,37 & 39 display the new 'Expanded' Patent
  Family table for UD=9216 and greater.  For more info. type ?NEWS351
  File 350:Derwent World Patents Index
         1963-1980, EQUIVALENTS THRU DW=9227
 **FILE350: Formats 32,33,35,37 & 39 display the new 'Expanded' Patent
  Family table for UD=9219 and greater.  For more info. type ?NEWS350

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            2945  ANTIBODIES/TI
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      S4      26  HUMANIS?
      S5       0  S4 AND (HUMANIZ? OR HUMANIS?)
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      S6   13936  ANTIBOD?
               1  S3
              26  S4
      S7       22  ANTIBOD? AND (S3 OR S4)
?ss cdr or (ig or immunoglobulin)()variable()region or (complementary()determing

Processing
Processing
      S8       31  CDR
      S9      786  IG
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     S10    1576  IMMUNOGLOBULIN
     S11  108404  VARIABLE
     S12  108131  REGION
     S13       4  (IG OR IMMUNOGLOBULIN)(W)VARIABLE(W)REGION
     S14   23564  COMPLEMENTARY
     S15     501  DETERMING
     S16       0  COMPLEMENTARY(W)DETERMING
     S17      23  HYPERVARIABLE
     S18  108131  REGION
     S19      12  (COMPLEMENTARY(W)DETERMING OR HYPERVARIABLE)(W)REGION
     S20   11218  ANTIBODY
     S21   43127  RELATED
     S22   28329  BINDING
     S23   29492  SITE? ?
     S24       0  ANTIBODY(W)RELATED(W)BINDING(W)SITE? ?
     S25      45  CDR OR (IG OR IMMUNOGLOBULIN)()VARIABLE()REGION OR
                  (COMPLEMENTARY()DETERMING OR HYPERVARIABLE)()REGION OR
                  ANTIBODY()RELATED()BINDING()SITE? ?
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              45  25
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?t26/7/1-8


 26/7/1     (Item 1 from file: 351)
009040436  WPI Acc No: 92-167794/21
XRAM Acc No: C92-077239
    New *humanised* *antibody* specific for interleukin-2 receptor - with
    complementarity determn. regions and framework from different
    immunoglobulin(s), is non immunogenic and used to treat T-cell
Patent Assignee: (PROT-) PROTEIN DESIGN LABS INC
Author (Inventor): QUEEN C L; SELICK H E
Number of Patents: 001
Number of Countries: 001
Patent Family:
    CC Number    Kind     Date      Week
    DD 296964       A5     911219     9221   (Basic)

Priority Data (CC No Date): DD 337159 (900117)
Abstract (Basic): DD 296964   A
        Compsn. comprises a practically pure human-type immunoglobulin
    (Ig) that reacts specifically with p55-Tac protein and/or inhibits
    binding of human interleukin-2 (Il-2) to its specific receptor.
              Also new are (1) human-type Ig having 2 pairs of light
    chain/heavy chain dimers and able to react specifically with an epitope
    of human IL-2 receptor with affinity at least 10 power 8 M-1, in which
    the complementarity determining regions (*CDR*) and human-type frame
    work regions are from different Ig molecules; (2) *humanised* Ig able
    to bind to IL-2 receptors with one or more *CDR* from anti-Tac
    *antibody* in a human framework, where the framework includes includes
    at least one amino acid (AA) from anti-Tac; (3) nucleic acid encoding a
    human Ig framework and murine *CDR* which, when expressed, produces an
    Ig specifically reactive with p55-Tac protein and can block binding of
    IL-2 to its receptor; (4) cells transformed with this nucleic acid.
              USE/ADVANTAGES - These Ig are used to treat humans with
    T-cell related diseases (e.g. transplant rejection; T-cell leukaemia or
    autoimmune diseases such as diabetes, multiple sclerosis, etc.). They
    are specific for the IL-2 receptors; are engineered to be
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non-immunising and can be produced by recombinant DNA method. The new Ig are admin. in usual parenteral formulation e.g. in doses of 150 mg for therapy or 0.5-2.5 mg for prophylaxis. Ig can also be used, opt. labelled, for diagnosis; T-cell typing; specific receptor isolation or vaccine prodn. 0/10

Derwent Class: B04; D16;
Int Pat Class: A61K-039/395; C12N-015/13

26/7/2 (Item 2 from file: 351)
009039793 WPI Acc No: 92-167155/20
XRAM Acc No: C92-076891

Prepn. of chimeric *humanised* *antibodies* - using a new polymerase chain reaction technique; PCR

Patent Assignee: (WELL) WELLCOME FOUND LTD
Author (Inventor): CROWE J S; LEWIS A P
Number of Patents: 001
Number of Countries: 015
Patent Family:

CC Number	Kind	Date	Week	
WO 9207075	A1	920430	9220	(Basic)

Priority Data (CC No Date): GB 9022011 (901010)
Applications (CC,No,Date): WO 91GB1744 (911008)
Language: English
EP and/or WO Cited Patents: 4.Jnl.Ref; WO 9007861
Designated States
(National): JP; US
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE

Abstract (Basic): WO 9207075 A

Prodn. of ds or ss DNA of formula: 5′ F1-M-F2 3′ encoding an *antibody* (Ab) chain or fragment in which at least one of the complementarily determining regions (CDRs) of the variable region is derived from a first mammalian Ab and the framework of the variable region is derived from a second different mammalian Ab, where M is DNA encoding a *CDR* of the second Ab and F1 and F2 resp. encode 5′ and 3′ sequences flanking M, by: (a) prepg. a ss or ds DNA template of formula: 5′ f1-H-f2 3′ where H is DNA encoding a *CDR* of a different specificity from M, and f1 and f2 are homologous to F1 and F2, resp.; (b) obtaining DNA oligonucleotide primers A, B, C and D, where: A comprises the sequence a1 with a 5′ end corresp. to the 5′ and of F1 and which is identical to the corresp. length of F1 and is oriented in a 5′ to 3′ direction towards H; B has of the sequence 5′ b1-b2 3′, where b1 comprises a sequence complementary to a corresp. length of M and has a 3′ end complementary to the 5′ end of M, and b2 is complementary to a sequence of corresp. length in F1 and has a 5′ end which starts at the nucleotide complementary to the 3′ end of F1, C has of the sequence 5′ c1-c2 3′ where c1 comprises a sequence identical to the corresp. length of M and has a 3′end corresp. to the 3′ end of M, and c2 is identical to a sequence of corresp. length in F2 and has a 5′ end which starts at the nucleotide corresp. to the 5′ end of F2, and D comprises a sequence d1 which has a 5′ end complementary to the 3′ end of F2 and which is complementary to a corresp. length of F2 and is oriented in a 5′ to 3′ direction towards H, where b1 and c1 overlap by a sufficient length to permit annealing of their 5′ ends under conditions which allow PCR to be performed; (c) performing, in any desired order, PCR reactions with primer pairs A, B and C, D on the template prepd. in (a), and (d) mixing the prods. of (c) and performing PCR using primers A and D.

USE/ADVANTAGE - The method allows the prepn. of chimeric, esp. *humanised* Abs. The resulting Ab retains the antigen binding

capability of the non-human Ab from which the *CDR*(s) are derived.
0/4
Derwent Class: B04; D16;
Int Pat Class: C12N-005/10; C12N-015/12; C12N-015/69; C12P-021/08

26/7/3 (Item 3 from file: 351)
008937440 WPI Acc No: 92-064709/08
XRAM Acc No: C92-029621
New multivalent anti-cytokine immunoglobulins - for treating disorders associated with elevated cytokine levels, e.g. septic and endotoxic shock, AIDS, allergies, etc.; ACQUIRE IMMUNE DEFICIENT SYNDROME
Patent Assignee: (CLLT) CELLTECH LTD; (CELL-) CELLTECH LTD
Author (Inventor): ALLEN R A; MORGAN S A
Number of Patents: 002
Number of Countries: 035
Patent Family:

CC Number	Kind	Date	Week	
WO 9201472	A	920206	9208	(Basic)
AU 9182381	A	920218	9222	

Priority Data (CC No Date): GB 9015908 (900719)
Applications (CC,No,Date): AU 9182381 (910719); WO 91GB1216 (910719)
Language: English
EP and/or WO Cited Patents: 2.Jnl.Ref; EP 347057; EP 355067; WO 9006371; WO 9007118; WO 9106305
Designated States
(National): AT; AU; BB; BG; BR; CA; CH; CS; DE; DK; ES; FI; GB; HU; JP; KP ; KR; LK; LU; MC; MG; MW; NL; NO; PL; RO; SD; SE; SU; US
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; OA; SE
Filing Details: AU9182381 Based on WO 9201472
Abstract (Basic): WO 9201472
New multivalent immunoglobulin (I) has at least 3 linked antigen-binding domains (ABD's) each being specific for a complementary site on a cytokine.
The combining interactions between ABD and cytokine sites are neutralising. (I) is specific for tumour necrosis factor (TNF) alpha or beta; an interleukin, an interferon or a colony-stimulating factor, and it contains 4-20 ABD.
ABD are all of class IgG (most pref.) or all of class IgM (but must be different from a native IgM molecule) and can be linked by covalent crosslinking (e.g. 2-iminothiolane/ maleimide system) or by non-covalent interaction (e.g. using an *antibody* reactive with sites on Ig other than those involved in antigen binding; or the biotin-avidin system). (I) are made by joining together appropriate immunoglobulin molecules or fragments esp *CDR*-grafted or *humanised* chimaeric Ig. USE/ADVANTAGE- (I) are used to treat or prevent diseases assciated with elevated cytokine levels, e.g. immuno regulatory and inflammatory disease, sepsis, endotoxic or cardiovascular shock, AIDS, psoriasis, organ transplant rejection or excessive TNF generation induced cancer therapy etc., Compared with monomeric Ig, (I) have much greater neutralising activity. @(43pp)@
Derwent Class: B04; D16;
Int Pat Class: A61K-039/39; A61K-039/395; C07K-015/28; C12P-021/08

26/7/4 (Item 4 from file: 351)
008929605 WPI Acc No: 92-056874/07
Related WPI Accession(s): 91-222915
XRAM Acc No: C92-025713
New *cdr*-grafted anti carcinoembryonic antigen *antibodies* - useful in therapy and diagnosis of carcinoma

Patent Assignee: (CELL-) CELLTECH LTD
Author (Inventor): ADAIR J R; BODMER M W; MOUNTAIN A; OWENS R J
Number of Patents: 001
Patent Family:

CC Number	Kind	Date	Week	
WO 9201059	A	920123	9207	(Basic)

Priority Data (CC No Date): WO 91GB1108 (910705); GB 9014932 (900705); WO 90GB2017 (901221)
Language: English
EP and/or WO Cited Patents: WO 8910140; WO 8901783; EP 323806; 6.Jnl.REF
Designated States
(National): AT; AU; BB; BG; BR; CA; CH; CS; DE; DK; ES; FI; GB; HU; JP; KP ; KR; LK; LU; MC; MG; MW; NL; NO; PL; RO; SD; SE; SU; US
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE; OA
Abstract (Basic): WO 9201059

New *humanised* *antibody* molecule (HAM) is specific for carcino-embryonic antigen (CEA) and has an antigen binding site in which at least one of the complementarity determining regions (*CDR*'s) of the variable domain is derived from the mouse monoclonal *antibody* (MAb) A5B7. The remaining Ig-derived parts of HAM are of human origin.

HAM is a chimeric or *CDR*-grafted *humanised* *antibody*, prepd. by recombinant DNA techniques. It can be a complete *antibody* or an Fab, Fab', (Fab')2 or Fv fragment, or a single-chain fragment. It may have a reporter or effector molecule attached to it.

USE/ADVANTAGE - HAM are useful in therapy or diagnosis (including imaging) of carcinomas which produce CEA, e.g., when coupled to a toxin such as ricin. @(70pp Dwg.No.0/19
Derwent Class: B04; D16;
Int Pat Class: A61K-039/39; C07K-015/28; C12N-015/13; C12P-021/08

26/7/5 (Item 5 from file: 351)
008849515 WPI Acc No: 91-353533/48
XRAM Acc No: C91-152448

New *humanised* *CDR*-grafted anti-ICAM *antibodies* - used to treat and prevent inflammation (e.g. psoriasis) tumours, viral infections and asthma and in diagnosis; INTER CELLULAR ADHESIVE MOLECULAR
Patent Assignee: (CELL-) CELLTECH LTD; (BOEH) BOEHRINGER INGELHEIM PHA
Author (Inventor): ADAIR J R; ATHWAL D S; ROTHLEIN R A
Number of Patents: 002
Patent Family:

CC Number	Kind	Date	Week	
WO 9116927	A	911114	9148	(Basic)
AU 9179001	A	911127	9210	

Priority Data (CC No Date): GB 909549 (900427)
Applications (CC,No,Date): WO 91US2942 (910429)
Language: English
EP and/or WO Cited Patents: US 4816567; WO 8901783; 7.Jnl.REF
Designated States
(National): AT; AU; BB; BG; BR; CA; CH; DE; DK; ES; FI; GB; HU; JP; KP; KR ; LK; MC; MG; MW; NL; NO; PL; RO; SD; SE; SU; US
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE; OA
Abstract (Basic): WO 9116927

A recombinant *antibody* molecule comprising antigen binding regions derived from the heavy and/or light chain variable regions of an anti-intracellular adhesion molecule-1 (anti-ICAM-1) *antibody* is claimed. The Ab is *CDR*-grafted and comprises several non-human residues. Also claimed are DNA encoding an Ab heavy or light chain, a vector comprising the DNA, host cells transformed with the vector and a method for producing the anti-ICAM-1 grafted Ab.

USE/ADVANTAGE - The Abs are used to treat - and prevent

inflammation in e.g. delayed type hypersensitivity, psoriasis, an autoimmune disease e.g. Reynaud7s syndrome, autoimmune thyroiditis, EAE, multiple sclerosis, rheumatoid arthritis and lupus erythematosus, tissue or organ transplant or graft rejection. They are also used to treat and prevent tumours, viral infections (e.g. rhinoviruses of the major serotype within the genus Picornavididae, group A coxsackievirus, a Mengo virus and HIV); asthma and non-specific defence system response, e.g. adult respiratory distress syndrome, CNS inflammatory disorder, multiple organ injury syndrome secondary to septicaemia or trauma, ulcerative colitis and Crohn's disease. Administration can be enteral, parenteral, topical, intranasal or by inhalation. The Abs are also used to diagnose an ICAM-1-expressing tumour cell and inflammation. @(68pp Dwg.No.0/4

Derwent Class: B04; D16;
Int Pat Class: A61K-039/39; C07K-015/28

26/7/6 (Item 6 from file: 351)
008718897 WPI Acc No: 91-222916/30
XRAM Acc No: C91-096865

CD3 specific *humanised* recombinant *antibody* - is chimeric or *cdr* grafted for immunotherapy and diagnosis; COMPLEMENTARY DETERMINE REGION

Patent Assignee: (CELL-) CELLTECH LTD
Author (Inventor): JOLLIFFE L K; ZIVIN R A; ADAIR J R; ATHWAL D S
Number of Patents: 003
Patent Family:

CC	Number	Kind	Date	Week	
WO	9109968	A	910711	9130	(Basic)
AU	9170330	A	910724	9143	
GB	2246781	A	920212	9207	

Priority Data (CC No Date): WO 90GB2018 (901221); GB 8928874 (891221); GB 9117611 (910815)
Applications (CC,No,Date): GB 9017611 (901221)
Language: English
EP and/or WO Cited Patents: EP 403156; EP 328404
Designated States (National): AT; AU; BB; BG; BR; CA; CH; DE; DK; ES; FI; GB; GR; HU; JP; KR ; LK; LU; MC; MG; MW; NL; NO; RO; SD; SE; SU; US
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE; OA
Filing Details: GB2246781 Based on WO9109968 (E) (1251CH)

Abstract (Basic): WO 9109968

A recombinant *antibody* (RAM) comprising antigen binding regions derived from the heavy and or light chain variable regions of a donor anti- CD3 *antibody*. The *antibody* preferably has binding affinity similar to that of OKT3. The RAM comprises antigen binding regions from suitable anti-CD3 *antibodies* such as rodent e.g. mouse or rat anti-CD3 MAb. The RAM may comprises only the variable region (VH and/or VL) or one or more CDRs of such a MAb.

The RAM is preferably a *humanised* *antibody* molecule specific for CD3 having an antigen binding site where at least one of the CDRs of the variable domain and usually two more of the CDRs are derviced from non human anti-CD3 *antibody*. The RAM may be a chimeric or *CDR* grafted *antibody*. Usually, the donor and acceptor *antibodies* are derived from different species. Typically the donor anti CD3 *antibody* is non-human (e.g. rodent) and the acceptor *antibody* is human. A *CDR* grafted *antibody* heavy chain comprising variable region with acceptor and donor CD3 binding comprising donor residues at one or more of positions 6, 37, 48 and 94. The *CDR* grafted light chain is also claimed.

DNA coding these *antibodies* and their production by recombinant DNA technology is claimed.

USE/ADVANTAGE - The *antibodies* may be used for treatment or diagnosis of human or veterinary conditions. The *humanised* *antibodies* do not have the immunologic complications associated with administration of non human *antibodies* to human subjects. @(81pp Dwg.No.0/13)@

Derwent Class: B04; D16;

Int Pat Class: A61K-039/39; A61K-049/00; C07K-015/06; C12N-005/10; C12N-015/13; C12P-021/08

26/7/7 (Item 7 from file: 351)

008718896 WPI Acc No: 91-222915/30

Related WPI Accession(s): 92-056874

XRAM Acc No: C92-025713

New *humanised* *antibodies* comprising *CDR* grafted *antibody* - with heavy and light chains, for use in vivo therapy and diagnosis; COMPLEMENTARY DETERMINE REGION

Patent Assignee: (CLLT) CELLTECH LTD; (CELL-) CELLTECH LTD

Author (Inventor): ADAIR J R; BODMER M W; MOUNTAIN A; OWENS R J; ATHWAL D S ; EMTAGE J S

Number of Patents: 005

Number of Countries: 035

Patent Family:

CC Number	Kind	Date	Week	
WO 9109967	A	910711	9130	(Basic)
AU 9169740	A	910724	9143	
GB 2246570	A	920205	9206	
WO 9201059	A	920123	9207	
AU 9182005	A	920204	9220	

Priority Data (CC No Date): GB 8928874 (891221); WO 90GB20174 (901221); GB 9014932 (900705)

Applications (CC,No,Date): AU 9182005 (910705); WO 91GB1108 (910705); GB 9017612 (901221)

Language: English

EP and/or WO Cited Patents: EP 239400; EP 323806; EP 328404; EP 403156; 6.Jnl.Ref; WO 8901783; WO 8910140

Designated States (National): AT; AU; BB; BG; BR; CH; DE; DK; FI; GB; HU; JP; KP; KR; LK; LU ; MC; MG; MW; NL; NO; RO; SD; SE; SU; US; CA; CS; ES; PL

(Regional): AT; BE; CH; DE; FR; GB; GR; IT; LU; NL; OA; SE; DK; ES

Filing Details: AU9182005 Based on WO 9201059

Abstract (Basic): WO 9109967

A *CDR* grafted *antibody* heavy chain is claimed having a variable region comprising acceptor frame-work and donor antigen binding regions in at least one of positions 6, 23 and/or 24, 48 and/or 49, 71 and/or 73, 75 and/or 76 and/or 78 and 88 and/or 91. Preferably, the heavy chain framework also comprises donor residues at positions 6, 37, 48 and 94. Also claimed is a *CDR*-grafted *antibody* light chain having a variable region domain comprising acceptor framework and donor antigen binding regions comprising donor residues in at least one of positions 1 and/or 3 and preferably at positions 46 and/or 47. A *CDR* grafted *antibody* molecule is also claimed comprising at least one *CDR* grafted heavy chain and light chain. DNA encoding the *CDR* grafted heavy and light chains is also claimed. The heavy or light chains may have an effector or reporter molecule attached e.g. a macrocycle for chelating a metal atom or a toxin such as ricin. The *CDR* grafted *antibodies* preferably have non-human e.g. rodent donor and human acceptor frameworkers.

USE/ADVANTAGE - For use in treatment and diagnosis of human and veterinary conditions. @(91pp Dwg.No.0/13

Derwent Class: B04; D16;
Int Pat Class: A61K-039/39; A61K-039/395; C07K-015/06; C07K-015/28; C12N-005/10; C12N-015/13; C12P-021/08; C12R-001/91

26/7/8 (Item 8 from file: 351)
008366799 WPI Acc No: 90-253800/33
XRAM Acc No: C90-109897
Chimaeric immunoglobulin(s) blocking IL-2 binding to receptors - comprising human framework and murine complementary determining regions, less immunogenic than murine *antibodies*
Patent Assignee: (PROT-) PROTEIN DESIGN LABS INC; (PROT-) PROTEIN DESIGN LABS
Author (Inventor): QUEEN C L; SELICK H E
Number of Patents: 010
Number of Countries: 034
Patent Family:

CC	Number	Kind	Date	Week	
WO	9007861	A	900726	9033	(Basic)
PT	92758	A	900629	9033	
CA	2006865	A	900628	9037	
AU	9051532	A	900813	9044	
ZA	8909956	A	901031	9048	
CN	1043875	A	900718	9115	
FI	9102436	A	910520	9133	
NO	9102385	A	910619	9142	
DK	9101191	A	910619	9143	
JP	4502408	W	920507	9225	

Priority Data (CC No Date): US 290975 (881228); US 310252 (890213)
Applications (CC,No,Date): WO 89US5857 (891228); JP 90503677 (891228); ZA 899956 (891228)
Language: English; German
EP and/or WO Cited Patents: 7.Jnl.Ref; EP 239400; GB 2188941; US 4816567; WO 8901783
Designated States
(National): AT; AU; BB; BG; BR; CH; DE; DK; FI; GB; HU; JP; KP; KR; LK; LU ; MC; MG; MW; NL; NO; RO; SD; SE; SU
(Regional): AT; BE; CH; DE; ES; FR; GB; IT; LU; NL; OA; SE
Filing Details: JP04502408 Based on WO 9007861
Abstract (Basic): WO 9007861

Compsn. comprises a pure human-like immunoglobulin (Ig) which (a) reacts specifically with p55 Tac protein and/or (b) inhibits binding of human interleukin-2 (IL-2) to its receptor. Also new are (1) human-like Ig having 2 pairs of light/heavy chains and able to react specifically with an epitope of a human IL-2 receptor with affinity at least 10 power 8 per mole, the chains including complementarily determg. regions (*CDR*'s) and human-like framework regions (FR's), the *CDR*'s being from different Ig molecules than FR's; (2) *humanised* Ig (hIg) which can bind to IL-2 receptors and contain at least one *CDR* from anti-Tac *antibody* in a human-like FR contg. at least one amino acid from the anti-Tac *antibody*; (3) nucleic acid encoding for human-like FR and at least one murine *CDR*, and (4) cells transfected with nucleic acid.

USE/ADVANTAGE - hIG are not significantly immunogenic in humans; are easily and economically produced, and have a longer half-life in vivo than mouse *antibodies*. They are useful (opt. when attached to a cytotoxic agent, for treatment of T-cell mediated disorders, e.g. graft or transplant rejection, and autoimmune diseases. LIG can also be used in vitro for T-cell typing; isolation of IL-2 receptor bearing cells, vaccine prodn., etc. @(52pp Dwg.No.0/10)@

Abstract (EP): 9142 EP 451216

Compsn. comprises a pure human-like immunoglobulin (Ig) which (a) reacts specifically with p55 Tac protein and/or (b) inhibits binding of human interleukin-2 (IL-2) to its receptor. Also new are (1) human like Ig having 2 pairs of light/heavy chains and able to react specifically with an epitope of a human IL-2 receptor with affinity at least 10 power 8 per mole, the chains including complementarily determg. regions (*CDR*'s) and human-like framework regions (FR's) the *CDR*'s being from different Ig molecules than FR's. (2) *humanised* IG (hIg) which can bind to IL-2 receptors and contain at least one *CDR* from anti-Tac *antibody* in a numan-like FR contg. at lesdt one amino acid from the anti-Tac *antibody*, (3) nucleic acid encoding for human-like FR and at least one murine *CDR*, and (4) cells transfected with nucleic acid.

USE/ADVANTAGE - hIG are not significantly immunogenic in humans, are easily and economically produced, and have a longer half-life in vivo than mouse *antibodies*. They are useful (opt. when attached to a cytotoxic agent, for treatment of T-cell mediated disorders, e.g. graft or transplant rejection, and autoimmune diseases, LIG can also be used in vitro for T-cell typing, isolation of IL-2 receptor bearing cells, vaccine prodn etc.

Derwent Class: B04; D16;

Int Pat Class: A61K-039/39; C07K-007/10; C07K-013/00; C07K-015/14; C12N-005/10; C12N-007/01; C12N-015/00; C12P-021/08

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COST       = OFF.
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HILIGHT set on as '*'
Hilight option is not available in file(s) 399.
?show files

File 155:MEDLINE_1966-1992/NOV (9211W1)
File   5:BIOSIS PREVIEWS_69-92/OCT BA9407:BARRM4307
         (C. BIOSIS 1992)
File  73:EMBASE (EXCERPTA MEDICA)_74-92/ISS37
         (COPR. ESP BV/EM 1992)
File 399:CA SEARCH_1967-1992 UD=11710
         (Copr. 1992 by the Amer. Chem. Soc.)
?ds


Set     Items   Description
S1         16   HUMANIZED()ANTIBODIES/TI
S2     332298   ANTIBODIES! FROM 155
S3       2253   IMMUNOGLOBULIN VARIABLE REGION! FROM 155
S4       2253   S2 AND S3
S5        862   HUMANIZ?
S6       2005   HUMANIS?
S7         16   S4 AND (HUMANIZ? OR HUMANIS?)
S8     636823   ANTIBOD? FROM 5,73,399
S9     165469   IMMUNOGLOBULIN
S10     41830   IG
S11    113462   VARIABLE
S12    392448   REGION
S13       862   (IMMUNOGLOBULIN OR IG)(W)VARIABLE(W)REGION
S14       604   CDR
S15     67991   COMPLEMENTARY
S16    112646   DETERMINING
S17        63   COMPLEMENTARY(W)DETERMINING
S18      1904   HYPERVARIABLE
S19    392448   REGION
S20       747   (COMPLEMENTARY(W)DETERMINING OR HYPERVARIABLE)(W)REGION
S21    428778   ANTIBODY
S22   1469126   RELATED
S23    623755   BINDING
S24    544344   SITE? ?
S25         0   ANTIBODY(W)RELATED(W)BINDING(W)SITE? ?
S26      2161   (IMMUNOGLOBULIN OR IG)()VARIABLE()REGION OR CDR OR (COMPLE-
              MENTARY()DETERMINING OR HYPERVARIABLE)()REGION OR ANTIBODY()R-
              ELATED()BINDING()SITE? ? FROM 5,73,399
S27       897   S8 AND S26
S28        18   S27 AND (S5 OR S6)
S29        34   S28 OR S7
S30        21   RD (unique items)
S31        21   Sort S30/ALL/PY,D
S32      3165   COMPLEMENTARITY
S33   2005813   DETERMIN?
S34    524927   REGION
S35       358   COMPLEMENTARITY(W)DETERMIN?(W)REGION
S36        12   COMPLEMENTARITY()DETERMIN?()REGION AND (S5 OR S6) AND S8
S37        28   7 OR 36
S38         8   (37 OR 29) NOT 29
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used complementary rather than complementarity in previous search.

Picked a few more references here.

S39 6 RD (unique items)
S40 6 Sort S39/ALL/PY,D
?t40/7/1-6

40/7/1 (Item 1 from file: 5)
9081780 BIOSIS Number: 93066780
DEVELOPMENT OF *HUMANIZED* BISPECIFIC *ANTIBODIES* REACTIVE WITH CYTOTOXIC LYMPHOCYTES AND TUMOR CELLS OVEREXPRESSING THE HER2 PROTOONCOGENE
SHALABY M R; SHEPARD H M; PRESTA L; RODRIGUES M L; BEVERLEY P C L; FELDMANN M; CARTER P
DEP. CELL BIOL., GENENTECH, INC., 460 POINT SAN BRUNO BOULEVARD, SOUTH SAN FRANCISCO, CALIF. 94080.
J EXP MED 175 (1). 1992. 217-226. CODEN: JEMEA
Full Journal Title: Journal of Experimental Medicine
Language: ENGLISH
The HER2 protooncogene encodes a 185-kD transmembrane phosphoglycoprotein, human epidermal growth factor receptor 2 (p185HER2), whose amplified expression on the cell surface can lead to malignant transformation. Overexpression of HER2/p185HER2 is strongly correlated with progression of human ovarian and breast carcinomas. Recent studies have shown that human T cells can be targeted with bispecific *antibody* to react against human tumor cells in vitro. We have developed a bispecific F(ab')2 *antibody* molecule consisting of a *humanized* arm with a specificity to 185HER2 linked to another arm derived from a murine anti-CD3 monoclonal *antibody* that we have cloned from UCHT1 hybridoma. The antigen-binding loops for the anti-CD3 were installed in the context of human variable region framework residues, thus forming a fully *humanized* BsF(ab')2 fragment. Additional variants were produced by replacement of amino acid residues located in light chain *complementarity* *determining* *region* 2 and heavy chain framework region 3 of the *humanized* anti-CD3 arm. Flow cytometry analysis showed that the bispecific F(ab')2 molecules can bind specifically to cells overexpressing p185HER2 and to normal human peripheral blood mononuclear cells bearing the CD3 surface marker. In additional experiments, the presence of bispecific F(ab')2 caused up to fourfold enhancement in the cytotoxic activities of human T cells against tumor cells overexpressing p185HER2 as determined by a 51Cr release assay. These bispecific molecules have a potential use as therapeutic agents for the treatment of cancer.

40/7/2 (Item 2 from file: 399)
117068366 CA: 117(7)68366p PATENT
Chimeric and complementarity-determining region-grafted anti-carcinoembryonic antigen antibodies and their production
INVENTOR(AUTHOR): Adair, John Robert; Bodmer, Mark William; Mountain, Andrew; Owens, Raymond John
LOCATION: UK,
ASSIGNEE: Celltech Ltd.
PATENT: PCT International ; WO 9201059 A1 DATE: 920123
APPLICATION: WO 91GB1108 (910705) *GB 9014932 (900705) *WO 90GB2017 (901221)
PAGES: 70 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12P-021/08A; A61K-039/395B; C12N-015/13B; C07K-015/28B DESIGNATED COUNTRIES: AT; AU; BB ; BG; BR; CA; CH; CS; DE; DK; ES; FI; GB; HU; JP; KP; KR; LK; LU; MC; MG; MN; MW; NL; NO; PL; RO; SD; SE; SU; US DESIGNATED REGIONAL: AT; BE; BF; BJ ; CF; CG; CH; CI; CM; DE; DK; ES; FR; GA; GB; GN; GR; IT; LU; ML; MR; NL; SE; SN; TD; TG
SECTION:
CA215003 Immunochemistry
IDENTIFIERS: carcinoembryonic antigen humanized chimeric antibody,

complementarity detg region grafted antibody CEA, cloning DNA humanized antibody CEA
DESCRIPTORS:
Antibodies,monoclonal...
A5B7 murine, to carcinoembryonic antigen, in humanized antibody prodn.
Animal cell line...
CHO L761 h, humanized anti-carcinoembryonic antigen antibody recombinant prodn. in
Deoxyribonucleic acid sequences...
for antibody variable regions in humanized anti-carcinoembryonic antigen antibody prodn.
Genetic vectors... Molecular cloning...
for humanized anti-carcinoembryonic antigen antibody prodn.
Diagnosis... Therapeutics...
humanized anti-carcinoembryonic antigen antibodies for
Escherichia coli...
humanized anti-carcinoembryonic antigen antibody fragment recombinant prodn. in
Animal cell line,CHO-K1... Animal cell line,COS-1... Bacteria...
humanized anti-carcinoembryonic antigen antibody recombinant prodn. in
Mammal...
humanized anti-carcinoembryonic antigen antibody recombinant prodn. in cells of
Immunoglobulins,fusion products...
humanized, prodn. of
Antibodies...
humanized, to carcinoembryonic antigen
Immunoglobulins...
in humanized anti-carcinoembryonic antigen antibody prodn.
Protein sequences...
of antibody variable regions in humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Eiisme...
pAL43, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pAL44, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pAL45, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pAL46, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pAL53, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pAL54, for humanized anti-carcinoembryonic antigen antibody prodn.
Genetic vectors...
pEE6hCMV gpt, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pHMC19, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pHMC30, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pHMC31, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pHMC43, for humanized anti-carcinoembryonic antigen antibody prodn.
Plasmid and Episome...
pHMC44, for humanized anti-carcinoembryonic antigen antibody prodn.
Genetic vectors...
pMRR028, for humanized anti-carcinoembryonic antigen antibody fragment prodn.

Genetic vectors...
pMRR045, for humanized anti-carcinoembryonic antigen antibody fragment prodn.
CAS REGISTRY NUMBERS:
142661-53-8 142661-54-9 142661-55-0 142661-56-1 142661-57-2
142661-58-3 amino acid sequence of, humanized anti-carcinoembryonic antigen antibody prodn. in relation to
142662-69-9 142662-70-2 142662-71-3 142662-72-4 142662-81-5
142662-82-6 nucleotide sequence of, humanized anti-carcinoembryonic antigen antibody prodn. in relation to

40/7/3 (Item 3 from file: 5)
8599131 BIOSIS Number: 92064131
IMMUNOGLOBULIN *COMPLEMENTARITY*-*DETERMINING* *REGION* GRAFTING BY RECOMBINANT POLYMERASE CHAIN REACTION TO GENERATE *HUMANIZED* MONOCLONAL *ANTIBODIES*
LEWIS A P; CROWE J S
DEP. CELL BIOLOGY, WELLCOME RES. LAB., LANGLEY COURT, BECKENHAM, KENT, BR3 3BS UK.
GENE (AMST) 101 (2). 1991. 297-302. CODEN: GENED
Full Journal Title: GENE (Amsterdam)
Language: ENGLISH
We describe an approach to rapidly generate *humanised* monoclonal *antibodies* by grafting rodent complementarity-determining regions into human immunoglobulin frameworks using recombinant polymerase chain reaction (PCR) methodology. The approach was applied to grafting a rat *complementarity*-*determining* *region* onto a human framework and amplifying the entire *humanised* heavy chain. The terminal oligodeoxyribonucleotide primers incorporated restriction sites to allow forced clonign into plasmid vectors for sequencing and expression. No nucleotide errors were introduced into the 1463-bp sequence even after sequential applications of PCR.

40/7/4 (Item 4 from file: 5)
7912269 BIOSIS Number: 40113269
CONSTRUCTION OF *HUMANIZED* *ANTIBODIES* AND TESTING IN PRIMATES
QUEEN C; CO M S; DESCHAMPS M; WHITLEY R; BENJAMIN W; HAKIMI J
PROTEIN DESIGN LAB. INC., 2375 GARCIA AVE., MOUNTAIN VIEW, CALIF. 94043.
MEETING ON MONOCLONAL ANTIBODIES HELD AT THE 20TH ANNUAL MEETING OF THE KEYSTONE SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, DENVER, COLORADO, USA, MARCH 10-16, 1991. J CELL BIOCHEM SUPPL 15 (PART E). 1991. 137. CODEN: JCBSD
Language: ENGLISH

40/7/5 (Item 5 from file: 5)
7400987 BIOSIS Number: 89052006
A *HUMANIZED* *ANTIBODY* THAT BINDS TO THE INTERLEUKIN 2 RECEPTOR
QUEEN C; SCHNEIDER W P; SELICK H E; PAYNE P W; LANDOLFI N F; DUNCAN J F; AVDALOVIC N M; LEVITT M; JUNGHANS R P; WALDMANN T A
PROTEIN DESIGN LABS., 3181 PORTER DRIVE, PALO ALTO, CALIF. 94304.
PROC NATL ACAD SCI U S A 86 (24). 1989. 10029-10033. CODEN: PNASA
Full Journal Title: Proceedings of the National Academy of Sciences of the United States of America
Language: ENGLISH
The anti-Tac monoclonal *antibody* is known to bind to the p55 chain of the human interleukin 2 receptor and to inhibit proliferation of T cells by blocking interleukin 2 binding. However, use of anti-Tac as an immunosuppressant drug would be impaired by the human immune response

against this murine *antibody*. We have therefore constructed a " *humanized*" *antibody* by combining the complementarity-determining regions (CDRs) of the anti-Tac *antibody* with human framework and constant regions. The human framework regions were chosen to maximize homology with the anti-Tac *antibody* sequence. In addition, a computer model of murine anti-Tac was used to identify several amino acids which, while outside the CDRs, are likely to interact with the CDRs or antigen. These mouse amino acids were also retained in the *humanized* *antibody*. The *humanized* anti-Tac *antibody* has an affinity for p55 of 3 .times. 109 M-1, about 1/3 that of murine anti-Tac.

40/7/6 (Item 6 from file: 399)
113170316 CA: 113(19)170316b PATENT
Recombinant antibodies to Campath-1 antigen, containing foreign complementarity determining region(s), and their use in immunosuppression and cancer therapy
INVENTOR(AUTHOR): Waldmann, Herman; Clark, Michael Ronald; Winter, Gregory Paul; Riechmann, Lutz
LOCATION: UK,
ASSIGNEE: Medical Research Council
PATENT: PCT International ; WO 8907452 A1 DATE: 890824
APPLICATION: WO 89GB113 (890210) *GB 883228 (880212) *GB 884464 (880225)
PAGES: 61 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-039/395A; C12N-015/00B DESIGNATED COUNTRIES: AU; DK; JP; US
SECTION:
CA215003 Immunochemistry
CA201XXX Pharmacology
CA203XXX Biochemical Genetics
IDENTIFIERS: chimeric antibody Campath 1 antigen, lymphoma neoplasm inhibitor Campath 1H antibody
DESCRIPTORS:
Rat...
complementarity detg. regions of, in recombinant antibody to Campath-1 antigen
Immunoglobulins,G2... Immunoglobulins,G3... Immunoglobulins,G4...
const. domains of human, in recombinant antibody contg. complementarity detg. regions to Campath-1 antigen
Lymphocyte...
depletion of, in human, by recombinant human antibody contg. foreign complementarity detg. regions to Campath-1 antigen
Gene and Genetic element,animal, synthetic...
for humanized light chain variable region, construction of, in prodn. of recombinant human antibody contg. rat complementarity detg. regions to Campath-1 antigen
Protein sequences...
of IgG2a YTH 34.5 HL heavy and light chain variable domains, of rat
Deoxyribonucleic acid sequences,IgG2a-specifying...
of rat
Antigens,CAMPATH-1...
recombinant antibodies to, foreign complementarity detg. regions in
Immunosuppressants... Neoplasm inhibitors... Neoplasm inhibitors,lymphoma ...
recombinant antibody contg. foreign complementarity detg. regions to Campath-1 antigen as
Gene and Genetic element,animal...
recombinant, for anti-Campath-1 antigen antibody of human, sequences encoding rat complementary detg. regions in
Immunoglobulins,G2a...
recombinant human antibody to Campath-1 antigen contg. complementary detg. regions of rat

Leukemia,B-cell...
recombinant human antibody to Campath-1 antigen killing leukemia cells of
Antibodies...
recombinant, to Campath-1 antigen, foreign complementarity detg. regions in
Immunoglobulins,G1... Immunoglobulins,G... Immunoglobulins,M...
recombinant, to Campath-1 antigen, foreign complementary detg. regions in
CAS REGISTRY NUMBERS:
129711-40-6 amino acid sequence encoded by HuVLLYS gene
129711-41-7 amino acid sequence encoded by synthetic HuVLLYS.degree. gene
129711-01-9 129711-02-0 cloning and nucleotide sequence of, of human and rat
129711-19-9 129711-20-2 cloning and nucleotide sequence of, of rat
128096-06-0 128096-07-1 128096-08-2 128096-09-3 128096-10-6 128096-11-7 complementarity detg. region of rat YTH 34.5 HL, human recombinant antibody contg., Campath-1 antigen binding by
129711-56-4 heavy chain variable region of human contg. rat complementarity detg. regions, recombinant antibody contg., Campath-1 antigen binding by
129711-60-0 heavy chain variable region of rat YTH 34.5 HL, recombinant antibody contg., Campath-1 antigen binding by
129710-86-7P HuVLLYS gene, prepn. of, in prepn. of recombinant human antibody contg. rat complementarity detg. regions to Campath-1 antigen
129711-59-7 light chain variable region of human contg. rat complementarity detg. regions, recombinant antibody contg., Campath-1 antigen binding by
129711-61-1 light chain variable region of rat YTH 34.5 HL, recombinant antibody contg., Campath-1 antigen binding by
127859-21-6P 127859-23-8P 127859-24-9P 127859-26-1P 127859-62-5P 127859-70-5P 127859-72-7P 127859-79-4P 127859-82-9P 127859-92-1P 127859-93-2P 127859-94-3P 127859-99-8P 127860-01-9P 127860-02-0P 127860-03-1P 127860-04-2P 129924-57-8P 129924-59-0P prepn. of, in gene synthesis for recombinant human antibody contg. rat complementarity detg. regions to Campath-1 antigen
129711-57-5 129711-58-6 recombinant human antibody contg., Campath-1 antigen binding by
129710-91-4P synthetic gene HuVLLYS.degree., prepn. of, in prepn. of recombinant human antibody contg. rat complementary detg. regions to Campath-1 antigen

?b351,350

15sep92 10:26:26 User209197 Session D127.2

SYSTEM:OS - DIALOG OneSearch
File 351:Derwent World Patents Index Latest
1981+;DW=9227,UA=9214,UM=9143
**FILE351: Formats 32,33,35,37 & 39 display the new 'Expanded' Patent Family table for UD=9216 and greater. For more info. type ?NEWS351
File 350:Derwent World Patents Index
1963-1980, EQUIVALENTS THRU DW=9227
**FILE350: Formats 32,33,35,37 & 39 display the new 'Expanded' Patent Family table for UD=9219 and greater. For more info. type ?NEWS350

Set	Items	Description

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Set     Items   Description
S1         22   ANTIBOD? AND (HUMANIS? OR HUMANIZ?)
S2          8   S1 AND (CDR OR (IG OR IMMUNOGLOBULIN)()VARIABLE()REGION OR
                 HYPERVARIABLE()REGION)
S3          0   S1 AND COMPLEMENTARITY()DETERMIN?()REGION
S4          3   S1 AND COMPLEMENT?()DETERMIN?()REGION
S5          1   (2 OR 4) NOT 2
?t5/7/1


 5/7/1     (Item 1 from file: 351)
007820291  WPI Acc No: 89-085403/11
XRAM Acc No: C89-037905
    Recombinant *humanised* *antibody* specific for TAG-72 - having
    complementarity determining regions of variable domains from mouse
    *antibody* and the remainder from human immunoglobulin
Patent Assignee: (CELL-) CELLTECH LTD
Author (Inventor): BODMER M W; ADAIR J R; WHITTLE N R
Number of Patents: 001
Patent Family:
    CC Number    Kind     Date      Week
    WO 8901783     A     890309     8911   (Basic)
Priority Data (CC No Date): WO 88GB731 (880905); GB 8720833 (870904)
Language: English
EP and/or WO Cited Patents: No.SR.Pub; 4.Jnl.REF
Designated States
 (National): AU; DK; FI; HU; JP; KR; NO; RO; SU; US
 (Regional): AT; BE; CH; DE; FR; GB; IT; LU; NL; SE
Abstract (Basic): WO 8901783
        A *humanised* *antibody* molecule (HAM) is claimed having
    specificity for the TAG-72 antigen and having an antigen binding site
    in which at least the *complementary* *determining* *region* (CDRs) of
    the variable domains are derived from the mouse monoclonal *antibodies*
    (MAb) B72.3 and the remaining immunoglobulin-derived parts of the HAM
    are derived from a human immunoglobulin.
        USE/ADVANTAGE - *Humanising* the B72.3 MAb does not adversely
    affect its binding activity and this produces a HAM which is useful in
    both therapy and diagnosis of certain carcinomas, e.g. solid tumours
    expressing TAG-72. @(49pp Dwg.No.0/13)@
Derwent Class: B04; D16;
Int Pat Class: A61K-039/39; C12N-015/00; C12P-021/00
?s complement?()determin?(w)region? ?

Processing
Processing
Processing
         27431  COMPLEMENT?
        234285  DETERMIN?
        124968  REGION? ?
     S6     23  COMPLEMENT?()DETERMIN?(W)REGION? ?
?c 1 and 6

            22  1
            23  6
     S7     10  1 AND 6
?

?c 7 not (2 or 4)
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              10  7
               8  2
               3  4
      S8       3  7 NOT (2 OR 4)
?t8/7/1-3


 8/7/1     (Item 1 from file: 351)
009004842  WPI Acc No: 92-132139/16
XRAM Acc No: C92-061892
    *Humanisation* of *antibodies* binding to human CD4 antigen - by
    mutation of framework-encoding regions of DNA encoding variable domain
    of rat or mouse *antibody* chain
Patent Assignee: (GORM/) GORMAN S D
Author (Inventor): CLARK M R; COBBOLD S P; GORMAN S D; WALDMANN H
Number of Patents: 001
Number of Countries: 018
Patent Family:
    CC Number    Kind     Date      Week
    WO 9205274      A      920402     9216   (Basic)

Priority Data (CC No Date): GB 9020282 (900917)
Applications (CC,No,Date): WO 91GB1578 (910916)
Language: English
EP and/or WO Cited Patents: 7.Jnl.Ref; EP 328404; EP 365209; EP 403156; WO
    9007861; WO 9107492; WO 9109966; WO 9109967
Designated States
 (National): AU; CA; JP; KR; US
 (Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE
Abstract (Basic): WO 9205274  A
         *Complementarity* *determining* *regions* (CDRs) of the variable
    domain of the *antibody* chain are derived from a first mammalian
    species and the framework of the variable domain and any constant
    domains of the Ab chain are derived from a second different mammalian
    species; comprising (a) mutating the framework-encoding regions of DNA
    encoding a variable domain of the first mammalian Ab chain such that it
    encodes the framework derived from the second species; and (b)
    expressing the Ab chain using this mutated DNA.
              The process specifically comprises: (i) determining
    nucleotide and predicted aminoacid sequence of a variable domain of a
    selected Ab chain of the first species; (ii) determining the Ab
    framework to which the framework of this domain is to be altered; (iii)
    mutating framework-encoding regions of DNA encoding this variable
    domain such that the mutated region encodes the framework determined in
    (ii); (iv) linking mutated DNA to DNA encoding a constant domain of the
    second species and cloning the DNA into an expression vector; and (v)
    introducing expression vector into a compatible host cell and culturing
    it to express Ab chain.
              USE/ADVANTAGE - Altered Abs is prepd., used to *humanise* an
    Ab, typically a monoclonal Ab and, e.g. a rat or mouse Ab. The
    resulting Ab retains the antigen binding capabilities of the Ab from
    which it is derived. Reshaped CD4 Ab is used to induce tolerance
    against an antigen. Used to alleviate autoimmune diseases e.g.
    rheumatoid arthritis, and to prevent graft rejection.  0/13
Derwent Class: B04; D16;
Int Pat Class: A61K-039/39; C12N-015/13; C12P-021/08

 8/7/2     (Item 2 from file: 351)
008712964  WPI Acc No: 91-216983/30
```

XRAM Acc No: C91-094177
Prodn. of *humanised* recombinant immunoglobulin - including polymerase chain reaction amplification of murine *antibody* light and heavy chain variable portions
Patent Assignee: (MERI) MERCK & CO INC
Author (Inventor): LAW M F; MARK G E; WILLIAMSON A R
Number of Patents: 002
Patent Family:

CC Number	Kind	Date	Week	
EP 438310	A	910724	9130	(Basic)
CA 2034553	A	910720	9139	

Priority Data (CC No Date): US 627423 (901220); US 467700 (900119)
Applications (CC,No,Date): EP 91300362 (910117)
Language: English
EP and/or WO Cited Patents: EP 239400; WO 8901783; 1.Jnl.REF
Designated States (Regional): CH; DE; FR; GB; IT; LI; NL
Abstract (Basic): EP 438310

Method for producing a *humanised* recombinant immunoglobulin comprises: (a) prepg. polymerase chain reaction (PCR) primers to amplify the variable portion of the light and heavy chain of a murine *antibody* which binds to a predefined antigen; (b) using the primers to amplify the variable portions of both heavy and light chains and sequencing the resulting nucleotide chains; (c) determining the murine *complementary* *determining* *regions* of the heavy and light chains; (d) selecting human variable heavy and light chain frameworks which show a high degree of amino acid similarity with the variable heavy and light chain framework of the murine immunoglobulin; (e) selecting human constant heavy and light chain frameworks; (f) grafting the murine *complementary* *determining* *regions* of (c) to the human framework regions of (e); (g) incorporating the complete DNA sequence for the *humanised* recombinant immunoglobulin into an appropriate expression vector; (h) transfecting host cells with the vector; (i) growing the transfected cells in an environment in which the *humanised* recombinant immunoglobulin is expressed; and (j) collecting the immunoglobulin.

A PCR method for the simultaneous synthesis and assembly of at least 4 deoxyoligonucleotides is also claimed.

USE/ADVANTAGE - The *humanised* recombinant immunoglobulins are weakly immunogenic or non-immunogenic when admin. to humans, and may be used as therapeutic agents. Recombinant human anti-CD18 *antibodies* or active fragments which bind to the CD18 antigen of leukocytes can be used to inhibit influx of the leukocytes into a site of inflammation or tissue liable to become inflamed following influx. @(78pp Dwg.No.0/38)@

Derwent Class: B04; D16;
Int Pat Class: C12N-015/13; C12P-021/08; C12Q-001/68

8/7/3 (Item 3 from file: 351)
007275804 WPI Acc No: 87-272811/39
XRAM Acc No: C87-115825
Recombinant altered *antibodies* - having *complementarity* *determining* *regions* replaced with those from *antibody* of different specificity
Patent Assignee: (WINT/) WINTER G P
Author (Inventor): WINTER G P
Number of Patents: 004
Patent Family:

CC Number	Kind	Date	Week	
EP 239400	A	870930	8739	(Basic)
GB 2188638	A	871007	8740	

JP 62296890 A 871224 8806
GB 2188638 B 900523 9021
Priority Data (CC No Date): GB 867679 (860327); GB 877252 (870326)
Applications (CC,No,Date): EP 87302620 (870326); JP 8773980 (870327)
Language: English
EP and/or WO Cited Patents: A3...8914; 3.Jnl.REF
Designated States
(Regional): AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
Abstract (Basic): EP 239400

An altered *antibody* in which at least parts of the *complementary* *determining* *regions* (CDRs) in the light or heavy chain variable domains have been replaced by analogous parts of CDRs from an *antibody* of different specificity is new.

The altered *antibody* can be produced by (a) prepg. a first replicable expression vector including a suitable promoter operably linked to a DNA sequence which encodes at least a variable domain of an Ig heavy or light chain, the variable domain comprising framework regions from a first *antibody* and CDRs comprising at least parts of the CDRs from a second *antibody* of different specificity, (b) if necessary, prepg. a second replicable expression vector including a suitable promoter operably linked to a DNA sequence which encodes at least the variable domain of a complementary Ig light or heavy chain, (c) transforming a cell line with the first or both prepd. vectors and (d) culturirg the transformed cell line to produce the altered *antibody*.

USE/ADVANTAGE - The method is used for ''*humanising*'' non-human monoclonal *antibodies* (MAbs) e.g. CDRs from mouse MAb can be partially or totally grafted into the framework regions of a human MAb, which is then produced in quantity by a suitable cell line. Only the CDRs of the *antibody* will be foreign to the body and this should minimise side effects if used for human therapy. @(41pp Dwg.No.0/8)@

Derwent Class: B04; D16;
Int Pat Class: C12N-015/00; C12P-021/02; C07K-015/00; A61K-039/39; C12N-005/00; C12R-001/91
?ds

Set	Items	Description
S1	22	ANTIBOD? AND (HUMANIS? OR HUMANIZ?)
S2	8	S1 AND (CDR OR (IG OR IMMUNOGLOBULIN)()VARIABLE()REGION OR HYPERVARIABLE()REGION)
S3	0	S1 AND COMPLEMENTARITY()DETERMIN?()REGION
S4	3	S1 AND COMPLEMENT?()DETERMIN?()REGION
S5	1	(2 OR 4) NOT 2
S6	23	COMPLEMENT?()DETERMIN?(W)REGION? ?
S7	10	1 AND 6
S8	3	7 NOT (2 OR 4)
S9	5	S1 AND CDRS
S10	0	(9 OR 7 OR 2 OR 4) NOT (7 OR 2 OR 4)

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